

Claim Rejections under 35 U.S.C. § 112, second paragraph

Claims 34 and 37 - 39 have been rejected as being indefinite. With respect to claims 34 and 37-39, the applicants have amended them according to the Examiner's suggestions as set forth in points 4a- 4d. Accordingly, Applicants respectfully request withdrawal of this ground of rejection.

Claim rejections under 35 U.S.C. § 103(a)

Claim Rejections under 35 U.S.C. § 103(a) over Brown et al. in view of Blanchard et al.

Rejection of 21, 22, 25, 29, 32-34, and 39

Claims 21, 22, 25, 29, 32-34, and 39 have been rejected under 35 U.S.C. 103(a) as obvious over Brown et al. (U.S. Patent No. 6,143,496) in view of Blanchard et al.

Applicants have carefully reviewed the Office Action and respectfully traverse the rejections for the following reasons. Reconsideration of the subject application in light of the present amendments and remarks is respectfully requested.

Applicants respectfully submit that none of the cited references disclose or suggest the present invention.

The Examiner alleges that Brown et al. teaches a method for reducing evaporation of a minute droplet of an aqueous solution. The Examiner acknowledges that Brown does not teach

delivery of an aqueous droplet onto the planar substrate using an inkjet technique; however, the Examiner alleges that it would have been obvious to combine the use of inkjet delivery technique taught by Blanchard et al. to the teachings of Brown.

Because Brown does not teach nor suggest the claimed invention, applicants submit that it would not have been obvious to combine the teachings of Brown with that of Blanchard to arrive at the present invention. The present invention is directed to a process for reducing evaporation or a process for conducting a PCR reaction in a minute droplet protected from evaporation in which the minute droplet is delivered into an oily liquid layer to contact a planar substrate using an inkjet technique. In the present invention, an oily liquid layer is provided on a planar first, and then a minute droplet of an aqueous solution is shot into the oily liquid layer, thereby effectively reducing evaporation of a minute droplet that would otherwise evaporate in several seconds. Brown, on the other hand, teaches providing a sample first on a substrate and then providing a displacing fluid. Further, Brown et al. teaches the use of a patterned layered substrate that includes patches of retaining material to retain a droplet. Thus, Brown fails to teach an effective method of reducing evaporation of a minute droplet that would otherwise evaporate in several second and does not teach nor suggest that the minute droplet be in contact with the surface of a planar substrate such as a glass slide. Therefore, even if Brown mentions using an ink jet technique for providing samples onto a substrate, it does not render the method of the present invention obvious. Furthermore, it would not be obvious to one skilled in the art to utilize the method of providing a sample by ink jet delivery as taught by Blanchard to modify the method of Brown. As previously discussed, Brown does not teach nor suggest providing an oily liquid layer on a planar substrate first, and then, shooting an aqueous solution into the oily

liquid layer. Additionally, applicants submit that Blanchard merely teaches using an ink jet technique for providing a small amount of samples onto well (P. 688, second column). Accordingly, applicants respectfully request withdrawal of this ground of rejection as Brown et al. do not render the claims obvious.

Regarding Claim 21, Brown et al. teaches the addition of a sample using a flow-through channel before providing displacing fluid to the assembly. (Col 8, lines 65- Col. 9, line 2) or using ink jet delivery using a microcapillary assemblies (Col. 20, lines 63 - Col. 21, line 10). Brown et al. provides a method for minimizing contamination by using one capillary tube for one sample and entrapping the sample inside the tube by sealing both ends of the tube. (Col. 20, lines 51 -55). Applicants respectfully submit that Brown et al. does not teach nor suggest adding an oily liquid layer to a planar substrate to reduce evaporation. Additionally, Brown et al. does not teach providing, by inkjet delivery, a minute aqueous droplet in the liquid layer as a means to reduce contamination by immobilizing and isolating the droplet on a planar substrate. Thus, applicants submit that Brown et al. does not render claim 21 obvious. Furthermore, it would not be obvious to one skilled in the art to utilize the method of providing a sample by ink jet delivery as taught by Blanchard to modify the method of Brown. As previously discussed, Brown does not teach nor suggest providing an oily liquid layer on a planar substrate first, and then, shooting an aqueous solution into the oily liquid layer. Additionally, applicants submit that Blanchard fails to teach providing an aqueous solution that is surrounded by Blanchard merely teaches using an ink jet technique for providing a small amount of sample onto wells. Therefore, Applicants submit that the combination of Brown in view of Blanchard does not render the claims obvious. Accordingly, applicants request withdrawal of this ground of rejection.

With respect to claim 22, the Examiner alleges that Brown teaches the use of a planar substrate that is water repellent. Applicants submit that Brown et al. teaches the use of a porous substrate that has a porous surface and does not teach nor suggest the use of a planar substrate that is water repellent. In contrast to Brown's porous substrate, the present invention provides a planar substrate that is water repellent in order to minimize spreading of the minute droplet on a planar substrate. The water repellent planar substrate allows the aqueous minute droplet to have a smaller area of contact with the planar substrate, and thus allows the minute droplet to rise in the thickness direction of the liquid layer, which in turn, provides a longer optical path and allows for easier optical detection. See page 5 of the specification. Thus, it would not be obvious to one of ordinary skill in the art to modify the method by replacing the porous substrate with a planar substrate that is water repellent because water repellency is not relevant to prevent spreading in a porous surface. Accordingly, applicants request withdrawal of this ground of rejection.

Regarding claim 25, the Examiner states that Brown et al. teaches layering an oily liquid layer on a planar substrate wherein the oily liquid layer is selected from mineral oil, silicon oil, and fluorinated oil. Applicant's submit that Brown teaches using a displacing fluid, that is introduced through flow-through channels, as a means for displacing the aqueous sample that is not held by a sample retaining means. In contrast, the present invention is directed to providing a planar substrate and an oily liquid layer and providing an aqueous minute droplet by shooting the minute droplet, using inkjet technique, into the oily liquid layer whereby the minute droplet contacts the planar substrate. Applicants respectfully submit that Brown et al. does not teach nor suggest adding an oily liquid layer to a planar substrate and shooting a minute droplet by inkjet

technique into the oily layer whereby the minute droplet contacts the planar substrate.

Accordingly, applicants request withdrawal of this ground of rejection.

Regarding Claim 29, the Examiner asserts that Brown et al. teaches covering the liquid layer with a cover. Applicants respectfully submit that Brown et al. does not teach nor suggest providing a covering over an oily liquid layer that surrounds all surfaces of a minute aqueous droplet that are not in contact with the planar substrate or the covering. Brown et al. teaches providing a cover that is attached by adhesive strips to the bottom portion of the assembly (Col. 27, line 34-37) whereas said bottom portion includes a patterned layer which faces the cover. The present invention teaches that by providing a cover to contact the upper surface of a minute droplet, one can elongate the optical path for facilitating optical measurements. Furthermore, Brown et al. does not teach nor suggest applying a cover in contact with said liquid layer contained on a planar substrate to elongate an optical path. Accordingly, applicants request withdrawal of this ground of rejection.

Regarding Claim 32, the Examiner asserts that Brown et al. teaches providing a patterned array comprising a plurality of minute droplets by providing a second aqueous solution into said oily layer whereby the second aqueous solution is adjacent to said first droplet. Applicants submit that Brown et al. teaches using screen printing and photolithography as methods to provide a patterned layer on the substrate that contains patches of isolated sample chambers (Col. 16, line 10-15). In contrast, the present invention does not require treating the substrate by screen printing or photolithography. Rather, the present invention is directed to providing a planar substrate and an oily liquid layer and providing an second aqueous minute droplet that is shot, by

inkjet technique, into the oily liquid layer whereby the second minute droplet is adjacent to a first minute droplet. Applicants respectfully submit that Brown et al. does not teach nor suggest adding an oily liquid layer to a planar substrate and shooting a second minute droplet by inkjet technique into the oily layer whereby the second minute droplet contacts the planar substrate and is adjacent to, but does not contact, a first minute droplet. Accordingly, applicants request withdrawal of this ground of rejection.

Regarding claims 33 and 34, the Examiner asserts that Brown et al. teaches a method for reducing evaporation of a minute droplet of an aqueous solution. Applicants submit that Brown et al. does not teach nor suggest providing a minute droplet by inkjet technique into an oily layer to contact a substrate, whereby the oily layer surrounds all surfaces of said droplet that are not in contact with the substrate. Furthermore, Brown et al. does not teach nor suggest applying a cover in contact with said liquid layer contained on a planar substrate to elongate an optical path. As such, applicants submit that Brown et al. do not render the present claims obvious. Furthermore, it would not be obvious to one skilled in the art to utilize the method of providing a sample by ink jet delivery as taught by Blanchard to modify the method of Brown. As previously discussed, Brown does not teach nor suggest providing an oily liquid layer on a planar substrate first, and then, shooting an aqueous solution into the oily liquid layer. Additionally, applicants submit that Blanchard fails to teach providing an aqueous solution that is surrounded by an oily liquid layer. Blanchard merely teaches using an ink jet technique for providing a small amount of sample onto wells. Therefore, Applicants submit that the combination of Brown in view of Blanchard does not render the claims obvious. Accordingly, applicants request withdrawal of this ground of rejection.

Regarding Claim 39, the Examiner alleges Brown et al. teaches an oily layer with a thickness of about 100 μm . In contrast, Brown teaches a flow-through channel that may have a preferred depth of from about 10 to 100 μm . Applicants submit that Brown et al. does not teach or suggest the use of an oily layer itself with a thickness of 100 μm as in the present invention directed to a planar substrate having an oily liquid layer of a thickness of 100 μm or less where an aqueous minute droplet is provided into the oily layer to contact a surface of the planar substrate. Accordingly, applicants request withdrawal of this ground of rejection.

Claim Rejection under 35 U.S.C. § 103(A) over Brown et al. in view of Blanchard et al. and Further in view of Sambrook et al.

Rejection of Claims 37 and 38

The Examiner asserts that although Brown et al. does not teach the method wherein the contact surface between said substrate and said droplet comprises the enzyme absorption preventing agent and the contact surface comprises a enzyme adsorption preventing agent or a bovine serum albumin coating, it would be obvious to one skilled in the art to utilize the methods of using to an enzyme adsorption preventing reagent as taught by Blanchard or by Sambrook to modify the method of Brown et al. As previously discussed, Brown et al. does not teach nor suggest providing an oily liquid layer on a planar substrate and shooting by inkjet technique a minute droplet into said layer such that said minute aqueous droplet is in contact with the planar substrate. Further, applicants submit that Blanchard et al. fails to teach providing a minute droplet into a liquid layer surrounding all surfaces of the minute droplet not in contact with the planar surface. Blanchard merely teaches using an ink jet technique for providing a small amount of sample onto wells (P. 688, Col. 2) Additionally, applicants submit that Sambrook et al. fails to teach providing a liquid layer surrounding all surfaces of a minute aqueous droplet not in contact with the planar substrate. Sambrook et al. merely teaches the use of various reagents, such as BSA, to block non-specific reactions. Applicants, therefore, submit that the combination of Brown et al. in view of Sambrook et al.'s disclosure fails to teach or suggest the present invention.

Applicants respectfully submit that Brown et al. in view of Blanchard and in view of Sambrook et al. does not render the claims obvious. Accordingly, applicants request withdrawal of this ground of rejection.

CONCLUSION

In view of the foregoing amendments and remarks, it is firmly believed that the subject invention is in condition for allowance, which action is earnestly solicited.

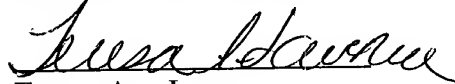
The Office is hereby authorized to charge Deposit Account No. 11-0600 with any additional fees required by this paper or credit any overpayment.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned directly at (202) 220-4258.

Entry of these claim amendments as well as prompt and favorable consideration of this Amendment is respectfully requested.

Respectfully submitted,

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MARKED UP VERSION OF AMENDED CLAIMS

34. (Five times Amended) A process for conducting a PCR reaction in a minute droplet of an aqueous solution protected from evaporation comprising the steps of:
- providing a planar substrate;
 - providing an oily liquid layer;
 - providing an aqueous solution immiscible with said oily liquid layer;
 - shooting a minute droplet by inkjet technique of said aqueous solution into said oily liquid layer to contact said planar substrate;
 - providing a covering in contact with said oily liquid layer;
- wherein said oily liquid layer surrounds all surfaces of said minute droplet of said aqueous solution that are not in contact with [said contact surface of] said planar substrate;
- providing to said [protected] minute droplet a reactant; and conducting a reaction in said [produced] minute droplet with said reactant whereby evaporation is reduced.
37. (Twice Amended) The process of claim 34 wherein [the] a contact surface between said substrate and said minute droplet comprises an enzyme adsorption preventing agent.
38. (Twice Amended) The process of claim 34 wherein [the] a contact surface between said substrate and said minute droplet comprises a bovine serum albumin coating.